

## ***Collaborating with the Global Supply Chain on Materials Requirements and a Rationalized Testing Paradigm***

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IPAC-RS Conference  
March 29-31, 2011 • Rockville Maryland

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## **Our Goal**

Is to improve the Quality and Integrity of the materials used in packaging and device manufacture, reduce supply chain problems and promote rational testing to support these ends.

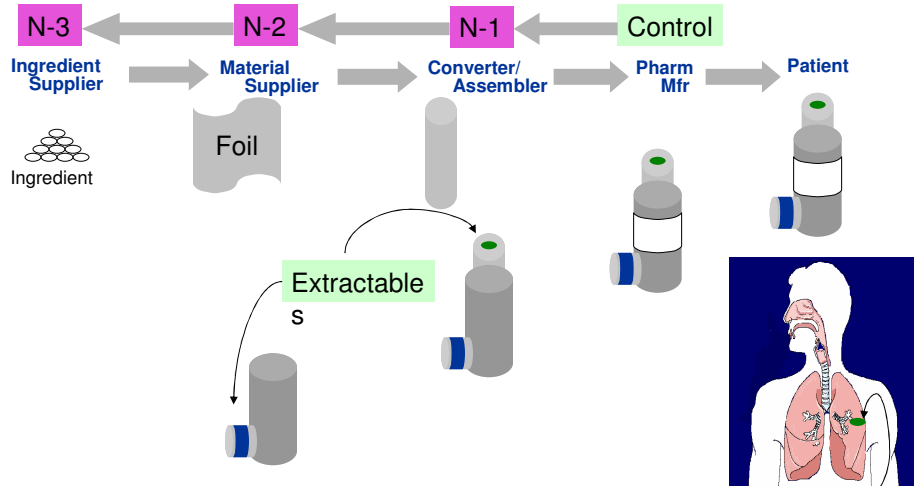
**The PATIENT is best served when we provide quality packaging and device components that are both safe and effective through the shelf life of the drug product.**



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## Quality Throughout the Supply Chain



Sources: Additives, Ambient Contaminants, Processing Aids



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Leachables

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## Risk associated with OINDP (US Perspective)

Table 1 Likelihood of Packaging Component-Dosage Form Interactions for Different Classes of Drug Products

Examples of Packaging Concerns for Common Classes of Drug Products

Degree of Concern Associated with the Route of Administration	Likelihood of Packaging Component-Dosage Form Interaction		
	High	Medium	Low
Highest	Inhalation Aerosols and Solutions; Injections and Injectable Suspensions*	Sterile Powders and Powders for Injection; Inhalation Powders	
High	Ophthalmic Solutions and Suspensions; Transdermal Ointments and Patches; Nasal Aerosols and Sprays		
Low	Topical Solutions and Suspensions; Topical and Lingual Aerosols; Oral Solutions and Suspensions	Topical Powders; Oral powders	Oral Tablets and Oral (Hard and Soft Gelatin) Capsules

Risk category

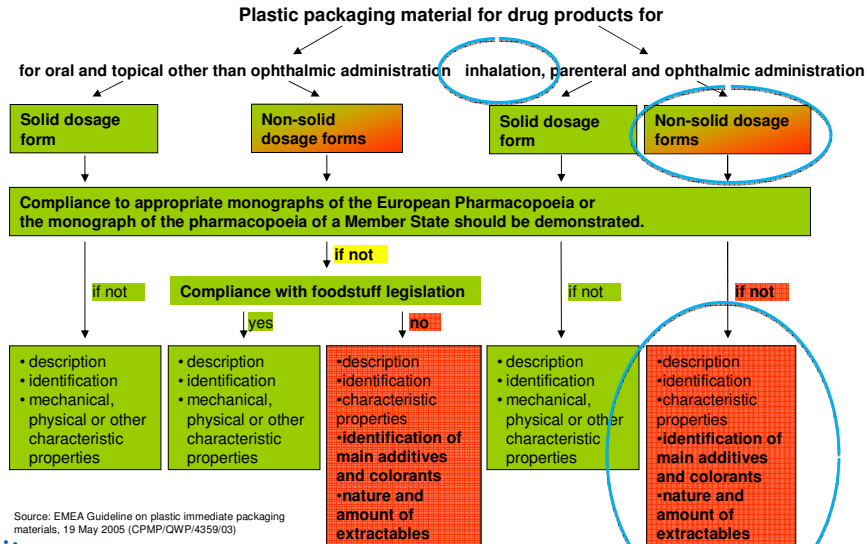
Extracted from 1999 FDA guidance document entitled "Container Closure Systems for Packaging Human Drugs and Biologics"



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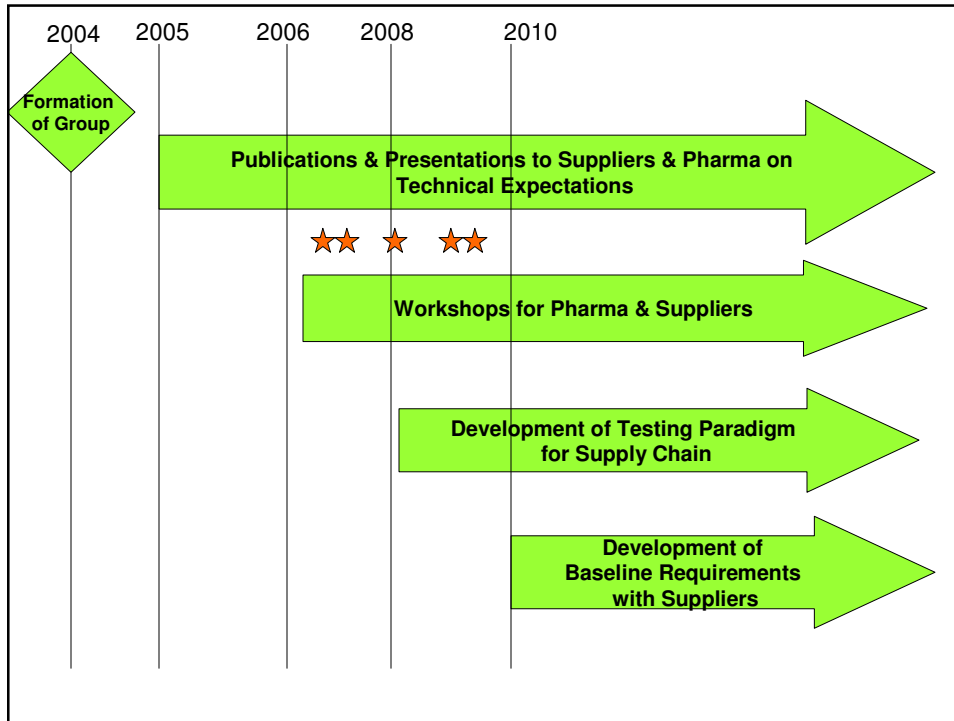
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## Risk associated with OINDP (EMEA Perspective)

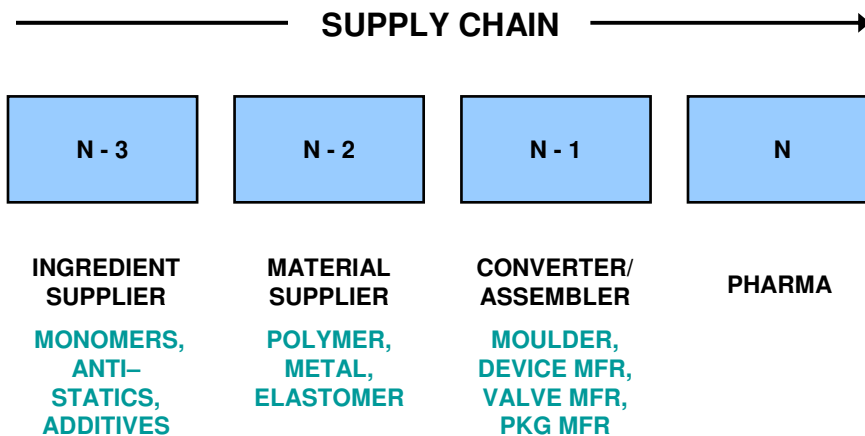


## IPAC-RS OINDP Materials Working Group; Background

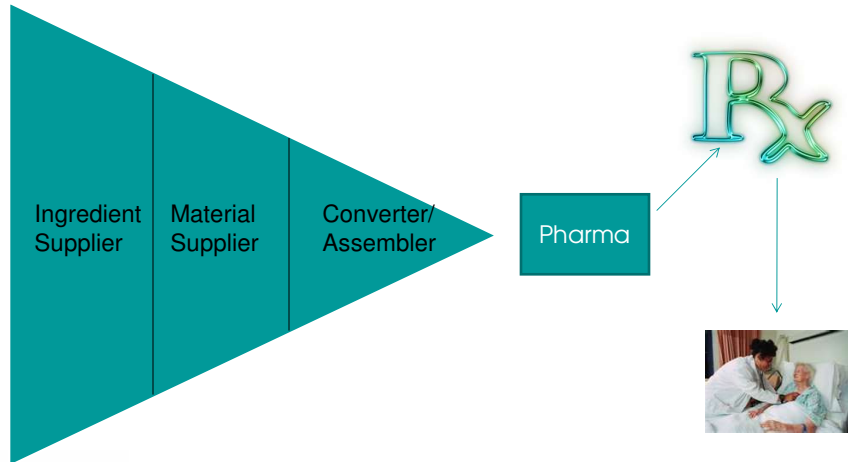
- Consideration of the PNA/nitrosamine question highlighted broader issues important not only to PNAs and nitrosamines in elastomers, but all extractables and component materials:
  - Varied perceptions of the extractables/leachables requirements for OINDP among Pharmaceutical Manufacturers and their Suppliers
  - Movement toward management of extractables and leachables using an information-rich, risk-based approach
  - Establishment of component quality beginning with material selection and support of robust quality systems throughout the supply chain



## Who makes up the supply chain to Pharma?

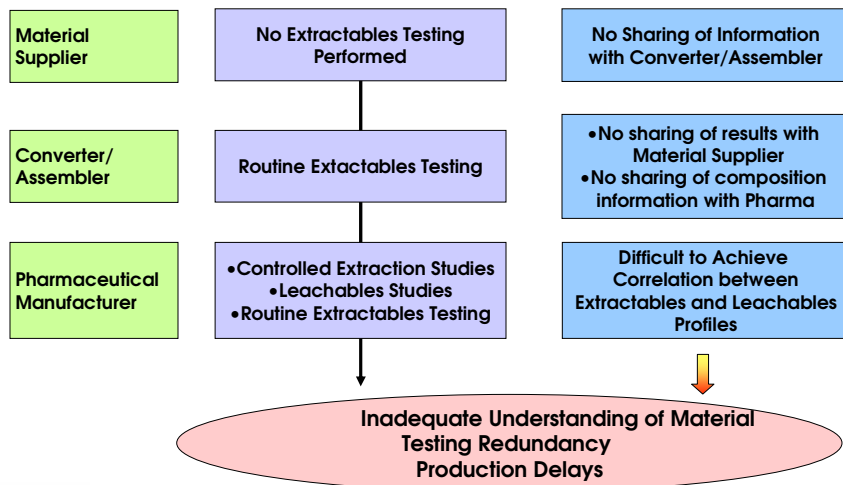


# What does the Supply Chain to the Patient Look Like?



# Testing Paradigm Circa 2005

## Scenario 1



## Material Testing – Regulatory Guidance

### Key Regulatory Guidance

- PQRI – Safety Thresholds & Best Practices For Extractables & Leachables in OINDP (Extractables/Leachables)
- Health Canada/EMA Guidance – Pharmaceutical Quality of Inhalation and Nasal Products (Extractables/Leachables)
- FDA - MDI/DPI Draft Guidance (Inhalation Product Performance & Characterization)
- FDA – Guidance on Inhalation solution, suspension, spray and nasal spray products
- CDRH - Reviewer Guidance for Nebulizers, Metered Dose Inhalers, Spacers and Actuators, (Product Characterization including Leachables)
- FDA - Guidance for Industry: Container Closure Systems for Packaging Human Drugs and Biologics (Packaging Characterization)
- CHMP, CVMP - Guideline for Plastic Immediate Packaging Materials (Packaging Characterization)
- EP 3, USP <381>, <661> (Physicochemical)
- ISO10993, USP<87>, USP<88> (Biocompatibility)



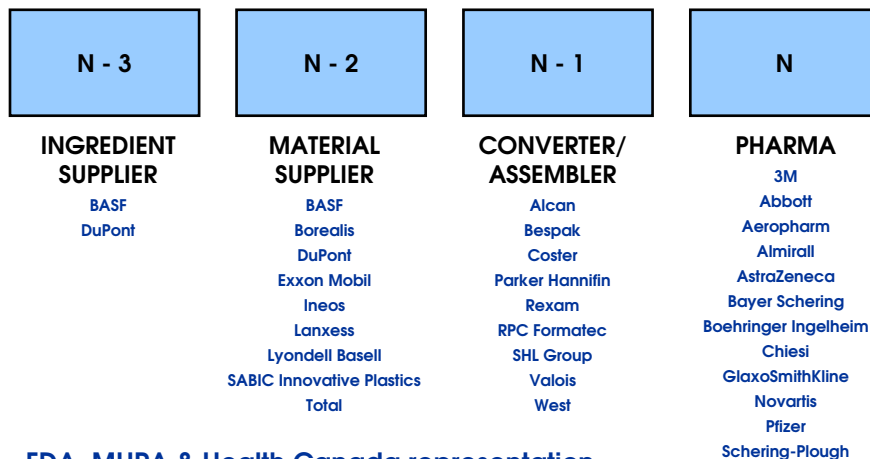
## 2009

The OINDP Materials Working Group held two Forums with Pharma, Suppliers (including N-1, N-2 and N-3 Suppliers) and Regulators to see if we could improve the communication and educational aspects of packaging and device manufacture. One Forum was held in Barcelona, Spain and the other in Philadelphia, Pennsylvania.



## Who Attended The Meetings?

### SUPPLY CHAIN →



FDA, MHRA & Health Canada representation



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## Discussion Point – What Does Pharma Need and Why?

### What....

Materials that meet functional/mechanical requirements

Materials that are safe for patients

### Why....

Understanding of compounds in materials that may reach the patient and may have consequences

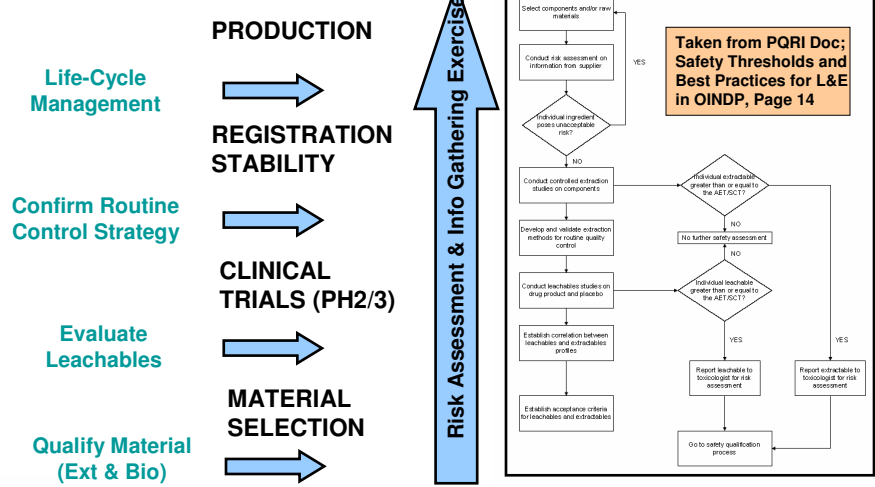
Material that is used in production is the same chemically as that which was used in the clinic so that there is assurance that the drug/pkg/patient interaction remains unchanged



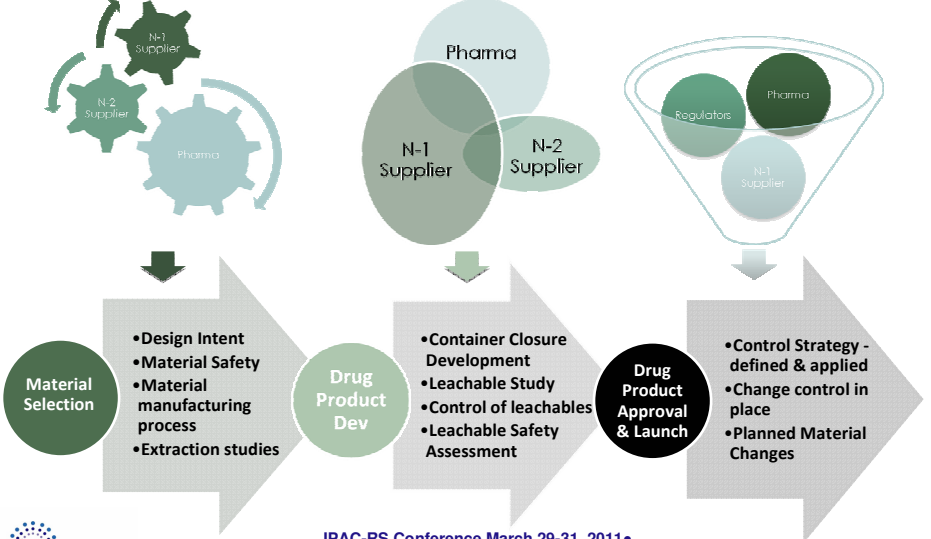
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# Testing & The Drug Product Development Process



# OINDP Materials Working Group Meets With The Supply Chain



## EU & US Forum Discussion Topics

- The following were discussed Enthusiastically

Communication

Breaking the Barriers

Confidential information/data

Can it be Shared?

Extraction & Biocompatibility studies

Who Conducts the testing?

Regulatory Expectations

What is Required for a Filing?

Lifecycle Management

Managing Post Approval Changes

Material Variability

What's Acceptable?

## Discussion Point – Extent & Type of Testing Throughout Supply Chain

### Raw Material Suppliers and Converter/Assembler

Provide Standard Testing information for their products:  
Functional/mechanical, biocompatibility, Food Grade

But had concerns about providing chemical testing data:  
Is there a Generic Extractables method ?  
Testing not representative of final product  
Customer Specific Methods  
Multiple components molded from the same batch of resin

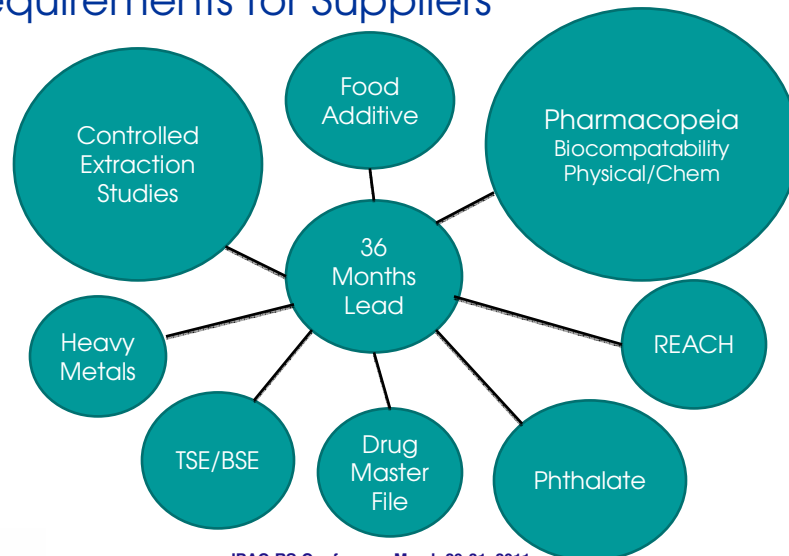
## Discussion Point – Extent & Type of Testing Throughout Supply Chain

### Pharma

We have to ensure to the PATIENT that:  
The product meets functional specifications

Material/Ingredient Changes post approval:  
Force Pharma to stockpile material in order to do the needed  
evaluation to the drug product  
New compounds above safety thresholds, but pose no tox concern  
will delay production

## So what was the outcome... Requirements for Suppliers



## Material Specification and What's in a Change?

- Specification is a Function of:
  - Attributes – (specific chemical, physical and mechanical functionality)
  - Test Methods
  - Acceptance criteria (providing the safety factor)

**And a change in these by any other name by the supplier, is still a change**



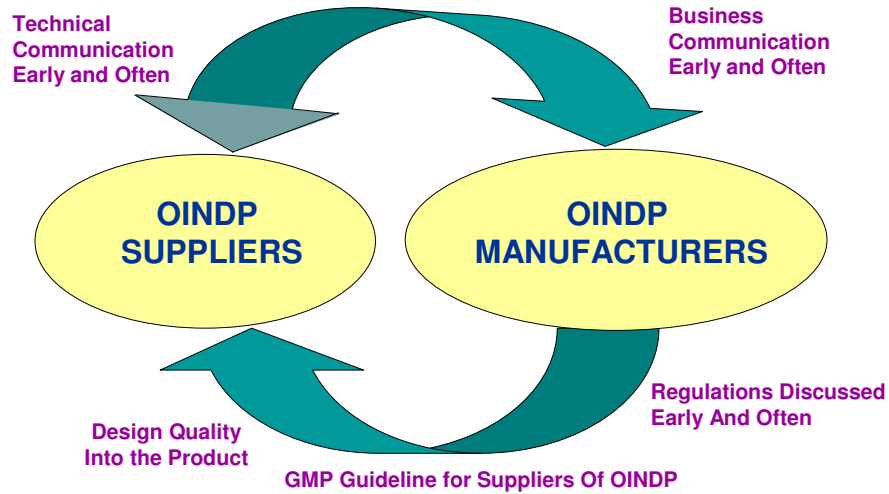
## These are change examples...

- Material composition—change of ingredient or supplier
- Material processing—change of conditions or processing aids
- Component processing—change of conditions, tooling or finishing steps

**Which must be discussed between Supplier and Pharma and a risk assessment performed.**

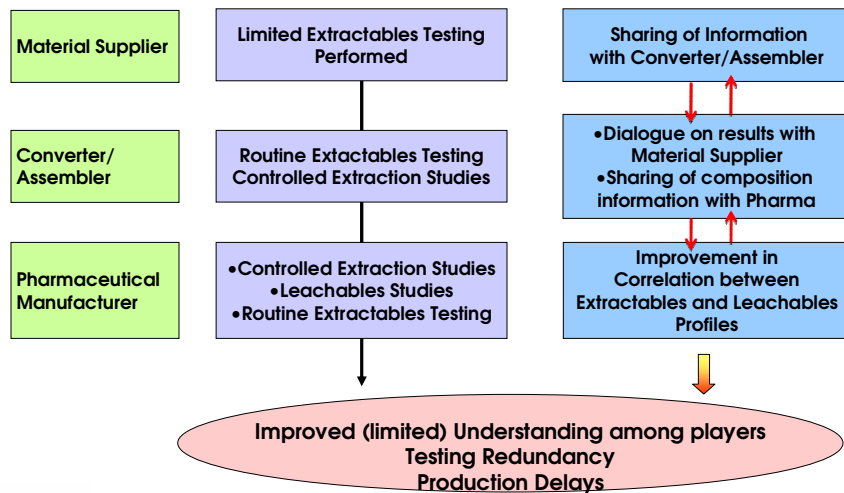


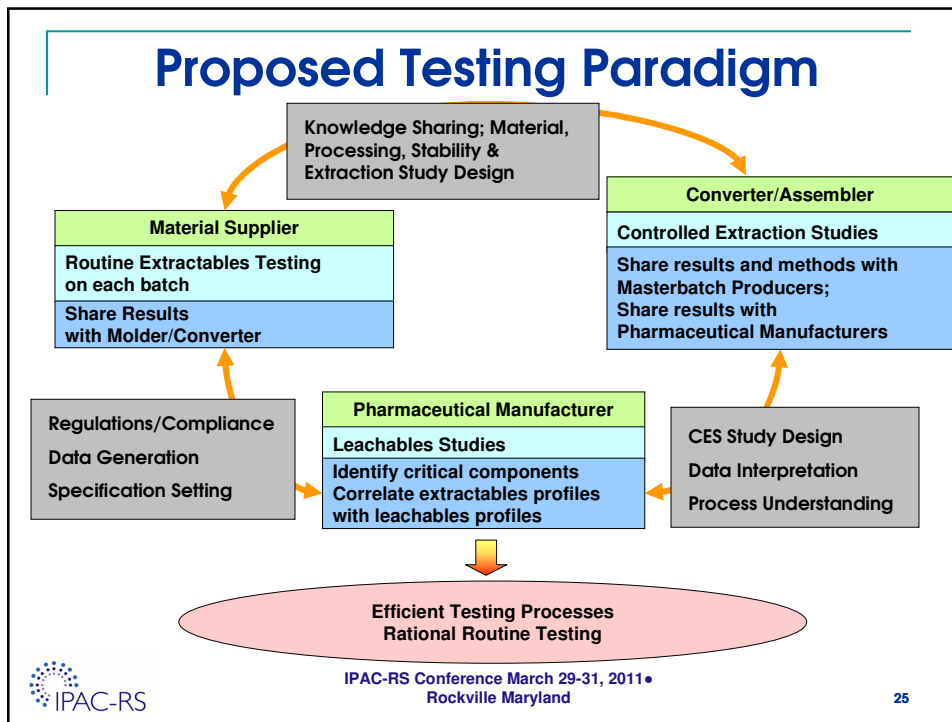
## OINDP Supplier & MFR Communication



## Current Testing Paradigm

### Scenario 1A





- ## How do We make the Paradigm a Reality for the Patient?
- We have open communication between all parties.
  - We understand business practices and have proper business agreements in place to exchange sensitive information
  - We share a set of baseline requirements
  - We establish Rational Specifications and Robust Change Control
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